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玻璃酸钠联合重组牛碱性成纤维细胞生长因子 对糖尿病性白内障超声乳化术后泪膜稳定性的影响*

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摘要 目的:探讨玻璃酸钠联合重组牛碱性成纤维细胞生长因子(bFGF)对糖尿病性白内障超声乳化术后泪膜稳定性的影响。**方法:**选取 2015 年 1 月到 2017 年 1 月期间在我院接受治疗的 150 例糖尿病性白内障患者,根据随机数字表法分为对照组和研究组,各 75 例。两组均进行常规治疗,在常规治疗的基础上对照组采用玻璃酸钠滴眼液进行治疗,研究组在对照组的基础上加用 bFGF 眼用凝胶进行治疗,两组均治疗 1 个月。比较两组术前、术后 1 周、术后 1 个月的泪膜破裂时间(BUT)、基础泪液分泌试验(SIt)值、角膜荧光素染色(FL)评分、干眼症状评分和眼表疾病指数(OSDI)评分,并比较两组术前、术后 1 个月的最佳矫正视力。**结果:**术后 1 周,两组患者的 BUT 明显低于术前和术后 1 个月,且研究组的 BUT 高于对照组($P<0.05$);随时间推移两组患者的 OSDI 评分持续降低($P<0.05$),术后 1 周,两组患者干眼症状评分、SIt 值、FL 评分明显高于术前和术后 1 个月,且研究组的 OSDI 评分、干眼症状评分、SIt 值、FL 评分均低于对照组($P<0.05$)。术后 1 个月两组患者的最佳矫正视力均明显上升,且研究组明显高于对照组($P<0.05$)。**结论:**玻璃酸钠联合 bFGF 能有效提升糖尿病性白内障患者在超声乳化术后泪膜稳定性,利于患者术后视力的恢复,值得临床推广应用。

关键词:玻璃酸钠;重组牛碱性成纤维细胞生长因子;白内障;糖尿病;泪膜

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Effect of Sodium Hyaluronate Combine with Recombinant Bovine Basic Fibroblast Growthfactor on Tear Film Stability after Phacoemulsification in Diabetic Cataract*

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ABSTRACT Objective: To investigate the effect of sodium hyaluronate combine with recombinant bovine basic fibroblast growthfactor (bFGF) on tear film stability after phacoemulsification in diabetic cataract. **Methods:** 150 patients with diabetic cataract who were treated in our hospital from January 2015 to January 2017 were treated. The patients were divided into the control group and the study group by random number table, each with 75 cases. Routine treatment was performed in the two groups, the control group was treated with sodium hyaluronate eye drops on the basis of routine treatment, the study group was treated with bFGF eye gel on the basis of the control group, the two groups were treated for 1 month. The break-up time (BUT), Schirmer test (SIt), corneal fluorescein staining (FL) score, symptoms of dry eye and ocular surface disease index (OSDI) score were compared between the two groups preoperation, 1 week after operation and 1 month after operation, and the best corrected visual acuity was compared between the two groups preoperation and 1 month after operation. **Results:** The BUT of the two groups was significantly lower at 1 week after operation than that at preoperation and 1 month after operation, and the BUT in the study group was higher than that in the control group ($P<0.05$). The OSDI scores of the two groups continued to decrease over time ($P<0.05$). The dry eye symptom score, SIt value and FL score of the two groups 1 week after operation were significantly higher than those at preoperation and 1 month after operation, and the OSDI score, dry eye symptom score, SIt value and FL score of the study group were lower than those of the control group ($P<0.05$). The best corrected visual acuity of the two groups increased significantly 1 month after operation, and the study group was significantly higher than that of the

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control group ($P<0.05$). **Conclusion:** Sodium hyaluronate combine with bFGF can effectively improve the tear film stability of patients with diabetic cataract after phacoemulsification, and it can be beneficial to the recovery of postoperative visual acuity, which is worthy of clinical application.

Key words: Sodium hyaluronate; Recombinant bovine basic fibroblast growth factor; Cataract; Diabetes mellitus; Tear film

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前言

白内障是指由老化、遗传、免疫及代谢异常、局部营养障碍、辐射等原因导致晶状体蛋白质发生变性混浊的眼病,可单眼发病,患眼的视力呈进行性减退,可出现眩光感、复视等症状,病情严重者可导致失明,严重影响患者的生活质量^[1-3]。糖尿病性白内障是糖尿病的常见并发症,主要是由于糖尿病患者会产生晶体无法排出的糖基化终产物(Advanced glycation end products, AGEs),导致 AGEs 在晶状体内堆积,最终引发糖尿病性白内障^[4-6]。超声乳化术是目前临床上治疗糖尿病性白内障的常用方法,具有较好的临床疗效,且患者术后视力恢复迅速、散光发生率低,但患者在术后易出现干眼症,同时易导致患者的泪膜稳定性下降,将对预后造成严重影响^[7-9]。玻璃酸钠是治疗干眼症的常用药,具有显著的亲水能力和润滑作用,可较好地缓解干眼症常见的烧灼感、异物感、干痒等临床症状^[10,11]。重组牛碱性成纤维细胞生长因子(Recombinant bovine basic fibroblast growth factor, bFGF)具有广泛的生物活性,角膜细胞、纤维细胞、血管内皮细胞、神经细胞、上皮细胞等细胞都能受这种多功能细胞生长因子刺激而生长^[12]。本研究旨在探讨玻璃酸钠联合 bFGF 对糖尿病性白内障患者在超声乳化术后泪膜稳定性的影响,以期为临床治疗超声乳化术后的不良反应提供参考,现报道如下。

1 资料与方法

1.1 一般资料

选取 2015 年 1 月到 2017 年 1 月期间在我院接受治疗的 150 例糖尿病性白内障患者,纳入标准:①均为假性糖尿病性白内障患者,其中糖尿病的诊断标准参照中华医学会糖尿病学分会制定的《中国 2 型糖尿病防治指南(2013 年版)》中的相关标准^[13],白内障参照世界卫生组织制定的白内障相关诊断标准^[14];②所有患者均符合超声乳化术的相关手术指征,并采用该手术进行治疗;③患者及其家属对本研究知情同意。排除标准:①1 型糖尿病患者;②合并有角膜炎、青光眼等其他眼部疾病者;③术前即存在明显的干眼症;④合并有严重器质性疾病、全身免疫性疾病以及恶性肿瘤者;⑤有眼部手术史、角膜接触镜佩戴史者。采用随机数字表法将患者分为对照组和研究组各 75 例。对照组男 39 例,女 36 例,年龄 47-85 岁,平均年龄(64.8 ± 6.9)岁,糖尿病病程 1-18 年,平均病程(4.7 ± 1.6)年,单眼发病 67 例,双眼发病 8 例。研究组男 38 例,女 37 例,年龄 43-87 岁,平均年龄(65.4 ± 6.4)岁,糖尿病病程 1-20 年,平均病程(4.4 ± 1.5)年,单眼发病 68 例,双眼发病 7 例。两组患者的一般资料无统计学差异($P>0.05$),本研究符合我院伦理委员会制定的相关规定,并已批准通过。

1.2 方法

1.2.1 手术方法 所有患者均给予超声乳化术进行治疗,术前 3d 滴加抗生素眼药水,并将血糖控制在正常范围,即糖化血红蛋白 $\leq 7\%$ 、空腹血糖 $\leq 8\text{ mmol/L}$,伴有高血压的患者进行降压处理,指导患者进行固视训练。行常规局部消毒,铺方巾,放置开睑器,采用盐酸奥布卡因进行表面麻醉,叮嘱患者术眼应注视显微镜发出的光源,以调整术中眼位,做 3 mm 的颞侧透明区角膜切口或反弧形巩膜隧道切口,将粘弹性物质注入,以保护角膜内皮,做直径 5 mm 左右的连续环形撕囊,采用劈裂技术及拦截劈裂技术乳化晶状体核,植入人工晶体。0.9%氯化钠注射液密封切口。

1.2.2 治疗方法 术后所有患者均采用妥布霉素地塞米松滴眼液(齐鲁制药有限公司,国药准字 H20020497,规格:每 5 mL 含妥布霉素 15 mg、地塞米松 5 mg)以及复方托吡卡胺滴眼液(沈阳兴齐眼药股份有限公司,国药准字:H20055546,规格:每 1 mL 含托吡卡胺 5 mg、盐酸去氧肾上腺素 5 mg)进行常规治疗,妥布霉素地塞米松滴眼液 4 次/d,每次 1 滴,复方托吡卡胺滴眼液 1 次/d,每次 1 滴。对照组在常规治疗的基础上加用玻璃酸钠滴眼液(参天制药株式会社,国药准字:J20130012,规格:0.3%(5 mL:15 mg),6 次/d,每次 1 滴。研究组在对照组的基础上加用 bFGF 眼用凝胶(珠海亿胜生物制药有限公司,国药准字 S20050100,规格:21000IU/5g/支),涂于眼部患处,早晚各 1 次。两组患者均连续治疗 1 个月。

1.3 观察指标

两组患者在术前、术后 1 周、术后 1 个月均进行泪膜破裂时间(Breakup time of tear film, BUT)、基础泪液分泌试验(Schirmer I test, SIt)、角膜荧光素染色(Fluorescein staining, FL)检测。其中 BUT 采用荧光素钠试纸进行检测,记录两组患者的 BUT, BUT 越短表示泪膜越不稳定;采用泪液试纸进行 SIt,记录两组患者泪液浸湿滤纸的长度,长度越长代表泪液在结膜囊的数量越多。采用荧光素钠试纸进行 FL 评分,将角膜分为 4 个象限,根据每个象限的染色程度进行评分,总得分为四个象限的得分之和,满分为 12 分,分数越高代表眼表损伤越严重。在术前、术后 1 周、术后 1 个月对两组患者进行干眼症状评分和眼表疾病指数(OSDI)评分。其中干眼症状主要通过患者有无出现眼异物感、干涩感、烧灼感、眼痒、视疲劳、眼痛、眼红、眼胀、畏光、视物模糊等情况,根据出现的强度和频率进行打分。若无明显不适,则记为 0 分,偶尔出现以上症状,则记为 1 分,间断出现且症状较严重,则记为 2 分,持续出现,且症状严重,则记为 3 分。OSDI 评分主要包含三个栏目,共 12 个题目,每个题目得分为 0-4 分,总分为 100 分,得分越高代表眼表状态越差。在术前、术后 1 个月采用自动电脑验光仪(Topcon, RM 8000)检测最佳矫正视力。

1.4 统计学方法

所有数据均用 SPSS19.0 进行统计分析, 计数资料和计量资料分别以率(%)、 $(\bar{x} \pm s)$ 的形式表示, 分别采用 χ^2 检验、t 检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者的 BUT、SIt、FL 比较

两组患者的 BUT、SIt 值、FL 评分在术前、术后 1 个月比较差异均无统计学意义($P > 0.05$)。术后 1 周, 两组患者的 BUT 明显低于术前和术后 1 个月, 且研究组的 BUT 高于对照组 ($P < 0.05$); 术后 1 周, 两组患者 SIt 值、FL 评分明显高于术前和术后 1 个月, 且研究组的 SIt 值、FL 评分比对照组低($P < 0.05$)。具体见表 1。

表 1 两组患者的 BUT、SIt、FL 比较($\bar{x} \pm s$)
Table 1 Comparison of BUT, SIt and FL between the two groups ($\bar{x} \pm s$)

Groups	Time	BUT(s)	SIt value(mm)	FL(score)
Control group(83 eyes)	Preoperation	8.12± 1.03	10.11± 1.13	3.43± 0.56
	1 week after operation	4.26± 1.37*	14.26± 1.21*	7.65± 0.61*
	1 month after operation	7.51± 1.14 [#]	11.06± 1.16 [#]	3.84± 0.56 [#]
Study group(82 eyes)	Preoperation	8.17± 1.04	10.08± 1.10	3.48± 0.54
	1 week after operation	5.67± 1.29* ^{&}	12.16± 1.18* ^{&}	5.12± 0.63* ^{&}
	1 month after operation	7.86± 1.33 [#]	10.53± 1.12 [#]	3.57± 0.51 [#]

Note: compared with preoperation, * $P < 0.05$; compared with 1 week after operation, [#] $P < 0.05$; compared with 1 month after operation, [&] $P < 0.05$.

2.2 两组患者干眼症状评分、OSDI 评分比较

两组患者的干眼症状评分、OSDI 评分在术前、术后 1 个月比较差异均无统计学意义 ($P > 0.05$)。随时间推移两组患者的

OSDI 评分持续降低($P < 0.05$), 术后 1 周, 两组患者干眼症状评分明显高于术前和术后 1 个月, 且研究组的干眼症状评分、OSDI 评分均比对照组低($P < 0.05$)。具体见表 2。

表 2 两组患者干眼症状评分、OSDI 评分比较($\bar{x} \pm s$)
Table 2 Comparison of dry eye symptom score and OSDI score between the two groups ($\bar{x} \pm s$)

Groups	Time	Dry eye symptom score(score)	OSDI(score)
Control group(83 eyes)	Preoperation	1.23± 0.35	30.45± 12.36
	1 week after operation	2.53± 0.41*	20.56± 10.23*
	1 month after operation	1.38± 0.37 [#]	10.15± 5.96 [#]
Study group(82 eyes)	Preoperation	1.25± 0.32	30.12± 12.13
	1 week after operation	1.91± 0.33* ^{&}	14.67± 8.67* ^{&}
	1 month after operation	1.22± 0.29 [#]	9.96± 5.36 [#]

Note: compared with preoperation, * $P < 0.05$; compared with 1 week after operation, [#] $P < 0.05$; compared with 1 month after operation, [&] $P < 0.05$.

2.3 两组患者最佳矫正视力比较

对照组术前和术后 1 个月的最佳矫正视力分别为(0.13± 0.01)、(0.54± 0.08), 研究组术前和术后 1 个月的最佳矫正视力分别为(0.12± 0.01)、(0.69± 0.12)。两组患者术前最佳矫正视力比较无差异($P > 0.05$), 术后 1 个月两组患者的最佳矫正视力均明显上升, 且研究组明显高于对照组($P < 0.05$)。

3 讨论

白内障是首要致盲眼病, 糖尿病性白内障是常见的一种白内障。近年来我国糖尿病患者的数量因国民生活水平提高和社会老年化不断增加, 糖尿病性白内障患者的数量也随之增加, 糖尿病性白内障已对患者视力构成严重威胁, 探究高效治疗糖尿病性白内障的方法具有重要的意义^[15-17]。糖尿病患者体内的血糖长期处于过高的状态, 其体内的蛋白质、氨基酸、脂类和核

酸等大分子物质的游离氨基与葡萄糖等还原糖分子中的醛基之间会发生缓慢而持久的反应, 形成 AGEs, 而晶体无法将 AGEs 排出, 使得其在细胞内积累, 导致晶状体颜色不断变混浊, 最终引发糖尿病性白内障^[18]。白内障超声乳化术是治疗白内障最常用的手术方法, 其具有无痛苦、时间短、切口小的特点, 但手术会破坏角结膜细胞, 进而降低了跨膜蛋白和黏蛋白的分泌, 同时手术也会造成角膜神经损伤, 导致瞬目次数减少、瞬目间歇时间增加, 进而使得患者出现眼部异物感、干涩感、烧灼感、眼红等症状^[19-21]。另一方面, 糖尿病患者通常泪液基础分泌量较正常人群更少、泪膜稳定性也更差, 且在进行超声乳化术后, 糖尿病患者会有较正常人群更加严重的炎症反应, 从而降低伤口愈合的速度, 因此超声乳化术后糖尿病性白内障患者的干眼症状更明显, 泪膜稳定性更差, 需要辅于相应的药物进行治疗^[22-24]。

BUT 是反映泪膜稳定常用的指标,可判断患者的泪液分泌是否不足,其数值越小干眼症状越严重。SIt 是检测水液层分泌不足型干眼症的常用检测方法,可反映泪液在结膜囊的数量。FL 可客观的评估眼表损伤的程度,进而间接反映出泪膜的稳定性。干眼症状评分以及 OSDI 评分是评价干眼症的常用评分量表,可反映干眼症的严重程度。在本次研究中,术后 1 周,两组患者的 BUT 明显低于术前和术后 1 个月,但研究组的 BUT 高于对照组($P<0.05$)。随着时间的推移两组患者的 OSDI 评分持续降低($P<0.05$),术后 1 周,两组患者干眼症状评分、SIt 值、FL 评分明显高于术前和术后 1 个月,且研究组的干眼症状评分、OSDI 评分、SIt 值、FL 评分低于对照组($P<0.05$)。这提示两组患者在术后均出现一定程度的干眼症状,且泪膜稳定性下降,而两种治疗方法均具有较好的治疗效果,但研究组患者在短期内的治疗效果更好,患者恢复更快。究其原因,玻璃酸钠滴眼液能起到保湿、抗炎的作用,同时能在角膜上形成保护膜,利于角膜细胞再生,促进伤口愈合。并且玻璃酸钠滴眼液的生物相容性以及亲水能力较好,可有效缓解药物刺激,并形成网状透气膜,帮助角膜细胞氧代谢保持正常^[25,26]。bFGF 能促进神经外胚层以及中胚层细胞的修复、再生,在超声乳化术后,bFGF 能有效促进角膜内皮层和基质层修复、角膜上皮的再生,同时 bFGF 可促进泪腺分泌,增加眼表的光滑程度,进而增加泪膜的稳定性^[27,28]。另外,末梢神经中存在大量 bFGF 受体,bFGF 可通过与其受体结合来促进神经再生,加速角膜知觉的恢复,进而提升泪膜的稳定性^[29]。本研究结果还显示,术后 1 个月两组患者的最佳矫正视力均明显上升,且研究组明显高于对照组($P<0.05$)。这提示研究组的治疗方法更利于视力的恢复,与金颖等人的研究结果相似^[30],bFGF 可修复角膜神经营养性上皮病变,能促进术后角膜知觉恢复,这可能是研究组患者视力恢复更好的原因。

综上所述,糖尿病性白内障患者在超声乳化术后泪膜稳定性下降,采用玻璃酸钠联合 bFGF 能有效改善患者的泪膜稳定性,利于患者术后视力的恢复,值得临床推广应用。

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